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Registration Decision RD2011-13

Lactobacillus casei strain LPT-111

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Registration Decision for *Lactobacillus casei* strain LPT-111

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of *Lactobacillus casei* Technical, Lacto-San-D and Lacto-San, containing the microbial pest control agent *Lactobacillus casei* strain LPT-111, to suppress various foliar diseases on field and greenhouse crops including roses, tomatoes, strawberries, cucumbers, grapes, squashes and pumpkins.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were proposed for full registration for the uses listed above in the consultation document[1] Proposed Registration Decision PRD2011-06, *Lactobacillus casei* strain LPT-111. This Registration Decision[2] describes this stage of the PMRA's regulatory process for *Lactobacillus casei* Technical, Lacto-San-D and Lacto-San and summarizes the Agency's decision. The PMRA received no comments on PRD2011-06. This decision is consistent with the proposed registration decision stated in PRD2011-06.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2011-06, *Lactobacillus casei* strain LPT-111 that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is *Lactobacillus casei* strain LPT-111?

Lactobacillus casei strain LPT-111 is a microbial pest control agent (MPCA) currently used as a commercial herbicide. Citric acid and lactic acid are organic acids that are fermentation products of the MPCA, and act as the active ingredients in two new end-use products, namely: Lacto-San and Lacto-San-D.

Lacto-San is a commercial product, while Lacto-San-D is a domestic product. Both products are used as bactericides/fungicides against various diseases (i.e., powdery mildew, downy mildew, bacterial cankers, black spot, and angular leaf spot) on a variety of outdoor and greenhouse crops, and ornamental roses. Lacto-San and Lacto-San-D have a low pH (~4.1). The citric and lactic acids produced during fermentation by *Lactobacillus casei* strain LPT-111 penetrate into the pathogen cell and disrupt cell homeostasis.

Health Considerations

Can Approved Uses of *Lactobacillus casei* strain LPT-111 and It's Fermentation Products, Citric Acid and Lactic Acid, Affect Human Health?

***Lactobacillus casei* strain LPT-111, and it's fermentation products citric acid and lactic acid, are unlikely to affect your health when Lacto-San and Lacto-San-D are used according to the label directions.**

People can be exposed to citric acid and lactic acid and the *Lactobacillus casei* strain LPT-111 when handling and applying Lacto-San and Lacto-San-D and when ingesting treated produce. When assessing the health risks associated with microbial active ingredients, several key factors are considered, such as: a microorganism's biological properties (for example, production of toxic byproducts), reports of any adverse incidents, potential to cause disease or toxicity as determined in toxicological studies and the level to which people may be exposed relative to exposures already encountered in nature to other isolates of this microorganism.

For biochemical actives, the levels where no health effects occur and the levels to which people may be exposed are also considered. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no adverse effects in animal testing are considered acceptable for registration.

Lactobacillus casei strain LPT-111 used in the manufacture of Lacto-San and Lacto-San-D, and the subsequent fermentation products (i.e., the organic acids), are already occurring in the food chain for human consumption at similar levels to those found in Lacto-San and Lacto-San-D. In addition, there have been relatively few reports of infection or adverse effects despite their ubiquity.

The active ingredients/fermentation products, citric and lactic acid, are of low acute toxicity by the oral route. Lactic acid is also of low acute toxicity via the dermal route; however, both lactic and citric acid are slightly irritating to the skin. Eye irritation studies indicated that, at the concentrations found in Lacto-San and Lacto-San-D, citric and lactic acid are capable of producing moderate to severe injury to the eye, particularly with repeated or prolonged exposure. Appropriate label statements and requirements for basic personal protective equipment will minimize impact for individuals with repeated or prolonged exposure.

Residues in Water and Food

Dietary risks from food and water are not of concern

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine whether the consumption of the maximum amount of residues, that are expected to remain on food products when a pesticide is used according to label directions, will not be a concern to human health. This maximum amount of residues expected is then legally established as a maximum residue limit under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act*. Health Canada sets science-based maximum residue limits to ensure the food Canadians eat is safe.

Lactobacillus casei strain LPT-111 is a strain of bacterium commonly used in the food industry to produce dairy products such as cheese and yogurt, and citric acid and lactic acid are naturally found in fruit as well as used as additives in beverages such as soft drinks. The levels of the MPCA and these organic acids that would result on food crops from the proposed use of Lacto-San and Lacto-San-D are expected to be much lower than levels already consumed in the Canadian diet from other sources. Therefore, the establishment of a maximum residue limit is not required for *Lactobacillus casei* strain LPT-111. As well, the likelihood of residues contaminating drinking water supplies is negligible to non-existent. Consequently, dietary risks are minimal to non-existent.

Occupational Risks From Handling Lacto-San and Lacto-San-D

Occupational risks are not of concern when Lacto-San and Lacto-San-D are used according to label directions, which include protective measures.

Workers using Lacto-San and Lacto-San-D can come into direct contact with *Lactobacillus casei* strain LPT-111, citric and lactic acid via the skin, in the eyes, or by inhalation. For this reason, the label will specify that commercial users exposed to Lacto-San must wear waterproof gloves, eye goggles, long-sleeved shirts, long pants, and shoes plus socks. Users are also directed to avoid inhaling the product and its mists. To reduce early-entry worker exposure, the commercial label will restrict workers from re-entering treated areas until the spray has dried. Standard precautionary label statements will warn domestic users of the potential for skin and eye irritation, but personal protective equipment is not required based on the infrequency of application of Lacto-San-D compared to commercial applicators.

Environmental Considerations

What Happens When Lacto-San and Lacto-San-D Are Introduced Into the Environment?

Environmental risks are not of concern.

Lactic acid bacteria, including *Lactobacillus casei,* are considered widespread in nature and are part of the commensal microflora of humans and animals as part of the gastrointestinal tract, oral cavity, and vagina. Published literature indicates that although foreign lactic acid bacteria can survive outside of the dairy environment they are unlikely to thrive there. As well, the number of *Lactobacillus casei* strain LPT-111 contained in Lacto-San and Lacto-San-D is very low and, therefore, the use of Lacto-San and Lacto-San-D is not likely to result in an increase of the number of *Lactobacillus casei* strain LPT-111 in the environment. Consequently, the risk to terrestrial and aquatic non-target organisms from the MPCA is negligible.

Citric acid and lactic acid readily undergo biotransformation in terrestrial and aquatic environments. Given the ubiquitous nature of citric and lactic acid in animals, plants, edible food commodities and industrial chemicals, the proposed uses of Lacto-San and Lacto-San-D on fruits, vegetables, and ornamental roses is not expected to result in a considerable increase in exposure to non-target terrestrial and aquatic organisms. Furthermore, reports in published literature of cases of adverse effects, as well as published toxicological endpoints, do not suggest that exposure of non-target terrestrial and aquatic organisms to the levels of citric and lactic acid in Lacto-San and Lacto-San-D will pose a concern with respect to toxicity. Based on the available data, citric acid and lactic acid are expected to pose negligible risk to terrestrial and aquatic organisms under conditions of use.

Value Considerations

What Is the Value of Lacto-San and Lacto-San-D

The Lacto-San end-use products and the acids they contains, which are produced by *Lactobacillus casei* strain LPT-111, are broad spectrum preventative fungicides and bactericides effective in the suppression of many important plant diseases.

The Lacto-San end-use products suppress commercially important fungal plant diseases including black spot on roses, downy mildew on cucumbers and powdery mildew on roses, strawberries, cucumbers, squashes and pumpkins. They have also been shown to have suppressive effects on bacterial diseases such as bacterial canker on tomatoes and angular leaf spot on strawberries. Because the Lacto-San products are manufactured in a food plant with only ingredients used for human consumption, the products represent a valuable reduced-risk alternative tool for disease management. In addition, the risk of disease resistance development by the target pathogens is assumed to be very low given the general nature of its putative mode of action, which includes physical exclusion, plasmolysis and membrane disruption of fungal cells.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the labels of Lacto-San and Lacto-San-D to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

To minimize exposure to *Lactobacillus casei* strain LPT-111, citric and lactic acid, all commercial applicators, mixer-loaders and handlers must wear waterproof gloves, long-sleeved shirts, long pants, shoes and socks and eye goggles. A label statement directing users to avoid inhaling the product and its mists is also included. Furthermore, to reduce early-entry worker exposure, the commercial label will restrict workers from re-entering treated areas until the spray has dried. Standard precautionary label statements will alert domestic users of the potential for skin and eye irritation.

Environment

As a general precaution from adverse effects on plants from high concentrations of acids, a precautionary statement will be imposed on the commercial and domestic end-use product labels warning users to follow mixing instructions carefully to ensure the product is properly diluted prior to application.

Furthermore, standard environmental precaution label statements to reduce runoff and to prevent handlers from contaminating aquatic habitats and systems will be added to the end-use product labels. Standard greenhouse label statements will also be added to advise users not to allow effluent or runoff from greenhouses to reach aquatic habitats.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2011-06, *Lactobacillus casei* strain LPT-111) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, healthcanada.gc.ca/pmra) or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

[5] As per subsection 35(1) of the *Pest Control Products Act*.